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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
12/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,065	LAUTT ET AL.	
	Examiner	Art Unit	
	Satyanarayana R. Gudibande	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-18,21-25 and 29-31* is/are pending in the application.

4a) Of the above claim(s) *7,18,22,29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6, 8-17, 21- 25 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group II invention (claims 6-8, 11, 29 and 30) and election of N-acetylcysteine and SIN-1 as species in the reply filed on 8/11/06 was acknowledged and the traversal arguments were answered in the office action dated 9/11/06.

Applicant's and remarks and amendment to claims in the response filed on 10/10/07 has been acknowledged.

Claims 6-18, 21-25 and 29-31 are pending.

Claims 7, 18, 22, 29 and 30 and have been withdrawn from further consideration as being drawn to non-elected species.

Claims 6, 8-17, 21-23, 24(in part to the extent that it reads on non-insulin dependent diabetes), 25 and 31 are examined on the merit.

Any objections and rejections made in the previous office action dated 7/23/07 and not specifically mentioned here are considered withdrawn.

Withdrawn Rejections

Claim Rejections - 35 USC § 112 first paragraph

Applicant's arguments, see pages 6-7, filed 10/10/07, with respect to the rejection(s) of claim(s) 6, 8-17, 21, 23, 24 (in part to the extent that it reads on non-insulin dependent diabetes), 25 and 29-31 under 35 USC 112, first paragraph have been fully considered and are persuasive.

Therefore, the rejection has been withdrawn. However, upon further consideration, grounds of rejections made under 35 USC 102(b) and 35 USC 103 made in the non-final action dated 9/11/06 have been reinstated as per the conditional withdrawal of the rejections stated in the office action dated 2/5/07.

The chronological events that require the office to reinstate the previous rejections made on 9/11/06 are as follows:

I. Applicants presented the following claim 6 for examination:

6. (Original) A pharmaceutical composition comprising a hepatic glutathione increasing compound and a hepatic nitric oxide-increasing compound.

The elected species N-acetylcysteine and SIN-1were found in a composition disclosed by US 6,436,996 B1 issued to Vitek, et al., and the claims were rejected under anticipation statute and under obviousness statute in view of references Mattia, et al., Diabetologia, 1998, 41, 1392-1396 and further in view of WO 00/19992 of Lautt, et al.

II. Applicants amended claim 6 on 12/11/06 to over come the rejections as follows:

6. (Currently Amended) A pharmaceutical composition comprising a combination of a therapeutically effective amount for reducing insulin resistance of a hepatic glutathione increasing compound and a therapeutically effective amount for reducing insulin resistance of a hepatic nitric oxide-increasing compound.

Office withdrew the rejections made under anticipation and obviousness statute with the following reasoning that appears on page 3 and 4 of the office action dated 2/5/07. The claims were rejected under 35 USC 112, first paragraph under new matter issues.

Applicants were put on notice that "**If the claims are again amended to overcome the new matter rejection original claim rejections under 35 U.S.C. 102(b) and 103 will be reinstated".**

III. In the currently amended form presented on 10/10/07, applicants present the following claim 6 for examination, stating that it conforms to examiner suggested claim structure:

6.(currently amended) A pharmaceutical composition comprising:

a) a therapeutically effective amount of hepatic glutathione increasing compound for reducing insulin resistance, ~~of a hepatic glutathione increasing compound~~ and

b) a therapeutically effective amount of hepatic nitric oxide increasing compound for reducing insulin resistance, ~~of a hepatic nitric oxide increasing compound.~~

The claim 6 as presented in the current amended form:

6. (currently amended) A pharmaceutical composition comprising:

a) a therapeutically effective amount of hepatic glutathione increasing compound for reducing insulin resistance~ ~~of a hepatic glutathione increasing compound~~ and

b) a therapeutically effective amount of hepatic nitric oxide increasing compound for reducing insulin resistance ~~of a hepatic nitric oxide increasing compound.~~

is anticipated by the previously cited reference of US 6,436,996 B1 issued to Vitek, et al., and under obviousness statute in view of references Mattia, et al., Diabetologia, 1998, 41, 1392-1396 and further in view of WO 00/19992 of Lautt, et al.

Therefore, the rejections made in the office action dated 9/11/06 are reinstated as per the afore-illustrated discussion. Rejections appear below.

Response to arguments

Applicants state that, "Although Applicants believe the Examiner is saying the same thing as the previous argument, Applicants have amended claim 6 to recite the Examiner's suggested claim structure".

Applicant's arguments filed 10/10/07 have been considered and have not been found persuasive. At no point did the office action suggest that the applicants amend the claims as currently amended.

Office made the following comment in the office action dated 7/23/07 but it was not a suggestion to amend the claims:

" A proper recitation of the claim 6 to correctly embody the **applicant's assertion** that the pharmaceutical composition comprising a hepatic glutathione increasing compound and a hepatic nitric oxide-increasing compound would be as follows:

A pharmaceutical composition comprising: a) a therapeutically effective amount of hepatic glutathione increasing compound for reducing insulin resistance, and b) a therapeutically effective amount of hepatic nitric oxide increasing compound for reducing insulin resistance".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6 and 8 rejected under 35 U.S.C. 102(b) as being anticipated by US 6,436,996 B1 issued to Vitek, et al.

In the instant application, applicants claim a pharmaceutical composition comprising of N-acetylcysteine and SIN-1 (elected species) as glutathione increasing and nitric oxide increasing compounds.

Vitek, et al., discloses such a composition comprising SIN-1 and N-acetylcysteine. Although, Vitek, et al., discloses the composition comprising of SIN-1 and N-acetylcysteine (claim 1, column 9, lines 5-8) as an exogenous source of increasing the nitric oxide levels in cells in Alzheimer's patients who suffer from decreased nitric oxide levels associated with the presence of APOE4 alleles, the composition comprises of the species elected in the present invention and hence, when administered, should perform the desired function of glutathione increasing and nitric oxide increasing functions (meeting the limitations of claim 6) in liver.

Further, the composition contains the presence of cysteine and dithiothreitol, which are known anti oxidants, meets the limitation of claim 8.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6, 8-17, 21-23, 24(in part to the extent that it reads on non-insulin dependent diabetes), 25 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,436,996 B1 issued to Vitek, et al., in view of Mattia, et al., Diabetologia, 1998, 41, 1392-1396 and further in view of WO 00/19992 of Lautt, et al.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

In the instant application, applicants claim a pharmaceutical composition comprising of N-acetylcysteine and SIN-1 and a method of administering the pharmaceutical composition for reducing insulin resistance in a mammalian patients having lower than normal glutathione

concentration wherein, N-acetylcysteine acts as glutathione increasing compound and SIN-1 acts as the nitric oxide increasing compound.

Vitek, et al., discloses composition containing the N-acetylcysteine and SIN-1 (claim 1, column 9, lines 5-8) as an exogenous source of increasing the nitric oxide levels in cells in Alzheimer's patients who suffer from decreased nitric oxide levels associated with the presence of APOE4 alleles. Even though the disclosed composition is for increasing the exogenous nitric oxide level in Alzheimer's patients, the disclosed composition will have desired inherent properties that cannot be precluded in the instant application since the compounds are same. The composition disclosed by Vitek, et al., meets the limitations of 6, 8, 14, 15, 21 and 23. The reference does not teach that the composition is for a method of reducing insulin resistance in a patient having lower than normal hepatic glutathione levels.

Mattia, et al., have shown that administration of N-acetylcysteine increases the glutathione and GSH/GSSG ratio concentration in non-insulin dependent diabetic patients (column 2 of 'summary' on page 1392). Lautt, et al., teaches the administration of nitric oxide increasing compounds such as SIN-1 stimulates nitric oxide in liver (abstract and page 8, lines 11-15) and provides a method for increasing insulin sensitivity (reducing insulin resistance). The reference of Mattia (column 2, page 1394 paragraph 1; and bridging paragraph on page 1395) and Lautt (pages 12-14) indicates that the respective compounds can be administered orally and intravenously (meeting the limitations of claims 16 and 17) to human patients. Lautt also describes the composition of the active ingredient along with other pharmaceutically acceptable carriers, diluents and adjuvants and vehicles (page 12, lines 4-17). The reference further

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Satyanarayana R. Gudibande, Ph.D.
Art Unit 1654

ANISH GUPTA
PRIMARY EXAMINER

discloses the use of targeted delivery systems such as vectors, liposomes, polymer matrices and microspheres (page 14, lines 7-13) meeting the limitations of claim 11.

It would have been obvious to one skilled in the art to combine the methods taught by Vitek, Mattia and Lautt to design a method for the treatment of non-insulin dependent diabetes. The motivation comes from the fact that the mechanism of non-insulin dependent diabetes involves both increase in glutathione concentration and a nitric oxide enhancement. Mattia teaches the use of N-acetylcysteine for increasing the glutathione concentration and Lautt teaches the use of SIN-1 for increasing the nitric oxide concentration in treating the non-insulin dependent diabetes. Even though Vitek used the combination of N-acetylcysteine and SIN-1 for a disease condition such as Alzheimer's, the reasonable expectation of success was provided by this reference. Vitek was successful in using the combination of the drugs to increase the nitric oxide levels in cells such as Alzheimer's disease. Therefore, the invention as a whole was clearly prima facie obvious to one skilled in the art at the time the invention was made. As set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980), "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; the idea of combining them flows logically from their having been individually taught in prior art."

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO